



UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Mark A. Dombroski et al.

Examiner: Evelyn Mei Huang

Serial No: 10/649,227

Art Unit: 1625

Filed: August 27, 2003

Docket: 17474 (PC25308A)

For: ALKYL-[4-(DIFLUOROPHENYL)-
OXAZOL-5-YL]-TRIAZOLO-
PYRIDINES

Confirmation No.: 5400

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, Virginia 22313-1450

DECLARATION OF DR. KIM F. MCCLURE

UNDER 37 C.F.R. §1.132

Sir:

I, Kim F. McClure, hereby declare as follows:

1. I am an applicant of U.S. Application Serial No.10/649,227, filed August 27, 2003, which claims the benefit of U.S. Serial No. 60/407,088, filed August 30, 2002;
2. I hold a Doctorate Degree in the field of Chemistry from Yale University which I obtained in 1993;
3. I have been employed at Pfizer, Inc. since 1995, and my current position is Senior Principal Scientist;
4. A true and correct copy of my Curriculum Vitae is enclosed herein as Exhibit A;

5. I have reviewed the above-identified application (hereinafter referred to as '227 application), and U.S. Patent No. 6,696,464 B2 (hereinafter referred to as the '464 patent) and I am familiar with the subject matter therein;

6. It is my scientific opinion that the two closest structural compounds between the '227 application and the '464 patent are 6-[4-(4-Fluoro-phenyl)-oxazol-5-yl]-3-isopropyl-[1,2,4]triazolo[4,3-a]pyridine (Example 12) in the '464 patent and 3-tert-Butyl-6-[4-(2,4-difluoro-phenyl)-oxazol-5-yl]-[1,2,4]triazolo[4,3-a]pyridine (Example 4) in the '227 application;

7. 6-[4-(4-Fluoro-phenyl)-oxazol-5-yl]-3-isopropyl-[1,2,4]triazolo[4,3-a]pyridine has a human whole blood TNF alpha IC₅₀ value of 685 nM;

8. 3-tert-Butyl-6-[4-(2,4-difluoro-phenyl)-oxazol-5-yl]-[1,2,4]triazolo[4,3-a]pyridine has a human whole blood TNF alpha IC₅₀ value of 76 nM;

9. It is my scientific opinion that the human whole blood TNF alpha IC₅₀ value of 76 nM for 3-tert-Butyl-6-[4-(2,4-difluoro-phenyl)-oxazol-5-yl]-[1,2,4]triazolo[4,3-a]pyridine shows that this compound is a surprisingly and unexpectedly better TNF alpha inhibitor than 6-[4-(4-Fluoro-phenyl)-oxazol-5-yl]-3-isopropyl-[1,2,4]triazolo[4,3-a]pyridine, which has a human whole blood TNF alpha IC₅₀ of 685 nM;

10. I declare that all statements made herein of my own knowledge are true and that all statements are believed to be true; and that those statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

By: Kim F McClure
Dr. Kim F. McClure

Dated: October 1, 2004

BEST AVAILABLE COPY

Vita for Kim F. McClure

Address:

Pfizer Inc
MS-8220-3228
Central Research Division
Eastern Point Road
Groton, CT 06340

Telephone:

(860) 441-8223

Facsimile:

(860) 715-4610

E-mail Address:

kim_f_mcclure@groton.pfizer.com

Social Security Number:

Date of Birth:

August 20, 1966

• **EDUCATION**

B.S. Chemistry, May 1988. University of California, Berkeley

Ph. D. Chemistry, December 1993. Yale University

• **EXPERIENCE**

Pfizer Inc., 1995-present. Senior Principal Scientist.

Post-doctoral Research Fellow (NIH), 1993-present, M.I.T. Advisor: Daniel S. Kemp
— Synthesis and study of α -helix templates and their peptide conjugates

Graduate Research Fellow, 1988–1993, Yale University. Advisor: Samuel J. Danishefsky
— Synthesis of FR-900482 congeners. Solid-phase carbohydrate synthesis using glycals.

Undergraduate research, 1987–88, U. C. Berkeley. Advisor: Clayton H. Heathcock
— Studies on zinc enolates. Synthesis of Daphnilactone A

Teaching Assistant, 1987–1990, Yale University (4 semesters); U.C.Berkeley (2 semesters)
— Introductory through graduate organic chemistry courses

• **AWARDS**

National Institutes of Health post-doctoral fellowship (1993–present)

Samuel K. Bushnell graduate fellowship (1989–1990)

Department of Education graduate fellowship (1990–1991)RFS

PUBLICATIONS

Reiter, Lawrence A.; Robinson, Ralph P.; McClure, Kim F.; Jones, Christopher S.; Reese, Matthew R.; Mitchell, Peter G.; Otterness, Ivan G.; Bliven, Marcia L.; Liras, Jennifer; Cortina, Santo R.; Donahue, Kathleen M.; Eskra, James D.; Griffiths, Richard J.; Lame, Mary E.; Lopez-Anaya, Arturo; Martinelli, Gary J.; McGahee, Shunda M.; Yocum, Sue A.; Lopresti-Morrow, Lori L.; Tobiassen, Lisa M.; Vaughn-Bowser, Marcie L. Pyran-containing sulfonamide hydroxamic acids: potent MMP inhibitors that spare MMP-1. *Bioorganic & Medicinal Chemistry Letters* 2004, 14, 3389-3395.

Dombroski, Mark A.; Letavic, Michael A.; McClure, Kim F.; Barberia, John T.; Carty, Thomas J.; Cortina, Santo R.; Csiki, Csilla; Dipesa, Alan J.; Elliott, Nancy C.; Gabel, Christopher A.; Jordan, Crystal K.; Labasi, Jeff M.; Martin, William H.; Peese, Kevin M.; Stock, Ingrid A.; Svensson, Linne; Sweeney, Francis J.; Yu, Chul H. Benzimidazolone p38 inhibitors. *Bioorganic & Medicinal Chemistry Letters* 2004, 14, 919-923.

Gale, Jeremy D.; McClure, Kim F.; Pullen, Nick. Emerging opportunities for the treatment of inflammatory bowel disease. *Annual Reports in Medicinal Chemistry* 2003, 38, 141-152.

Letavic, Michael A.; Axt, Matt Z.; Barberia, John T.; Carty, Thomas J.; Danley, Dennis E.; Geoghegan, Kieran F.; Halim, Nadia S.; Hoth, Lise R.; Kamath, Ajith V.; Laird, Ellen R.; Lopresti-Morrow, Lori L.; McClure, Kim F.; Mitchell, Peter G.; Natarajan, Vijayalakshmi; Noe, Mark C.; Pandit, Jayvardhan; Reeves, Lisa; Schulte, Gayle K.; Snow, Sheri L.; Sweeney, Francis J.; Tan, Douglas H.; Yu, Chul H. Synthesis and biological activity of selective pipecolic acid-based TNF- α converting enzyme (TACE) inhibitors. *Bioorganic & Medicinal Chemistry Letters* 2002, 12, 1387-1390.

Rohde L.E.; Ducharme A.; Arroyo L.H.; Aikawa M.; Sukhova G.H.; Lopez-Anaya A.; McClure K. F.; Mitchell P.G.; Libby P.; Lee R.T. *Circulation* 1999, 99, 3063-3070. Matrix metalloproteinase inhibition attenuates early left ventricular enlargement after experimental myocardial infarction in mice.

McClure, K. F.; Axt, M. Z. *Bioorg. & Med. Chem. Lett.* 1998, 8, 143. Alkylation of Succinates: Synthesis of Ro 32-3555.

Groebke, K.; Renold, P.; Tsang, K. Y.; Allen, T. J.; McClure, K. F.; Kemp, D. S. *Proc. Natl. Acad. Sci. U.S.A.* 1996, 93, 4025. Template-nucleated Alanine-Lysine helices are Stabilized by Position-dependent Interactions Between the Lysine Side Chain and the Helix Barrel.

Cammers-Goodwin, A.; Allen, T. J.; Oslick, S. L.; McClure, K. F.; Lee, J. H.; Kemp, D. S. *J. Am. Chem. Soc.* 1996, 118, 3082. Mechanism of Stabilization of Helical Conformations of Polypeptides by Water Containing Trifluoroethanol.

Randolph, J. T.; McClure, K. F.; Danishefsky, S. J. *J. Am. Chem. Soc.* 1995, 117, 5712. Major Simplifications in Oligosaccharide Syntheses Arising From A Solid-Phase Based Method: An Application to the Synthesis of the Lewis b Antigen.

McClure, K. F.; Renold, P.; Kemp, D. S. *J. Org. Chem.* 1995, 60, 454. An Improved Synthesis of a Template for α -Helix Formation.

McClure, K. F.; Danishefsky, S. J.; Schulte, G. K. *J. Org. Chem.* 1994, 59, 355. A Remarkable Inversion in Some Heck Arylation Reactions. A Mechanistic Proposal.

Benbow, J. W.; McClure, K. F.; Danishefsky, S. J. *J. Am. Chem. Soc.* 1993, 115, 12305. Intramolecular Cycloaddition Reactions of Dienyl Nitroso Compounds: Application to the Synthesis of Mitomycin K.

McClure, K. F.; Danishefsky, S. J. *J. Am. Chem. Soc.* 1993, 115, 6094. A Novel Heck Arylation Reaction: Rapid Access to Congeners of FR 900482.

Danishefsky, S. J.; McClure, K. F.; Randolph, J. T.; Ruggeri, R. B. *Science (Washington, D.C.)* 1993, 260,

BEST AVAILABLE COPY

Vita for Kim F. McClure

1307. A Strategy for the Solid-Phase Synthesis of Oligosaccharides.

Heathcock, C. H.; Ruggeri, R. B.; McClure, K. F. *J. Org. Chem.* 1992, 57, 2585. *Daphniphyllum* Alkaloids. 15. Total Synthesis of (\pm)-Methyl Homodaphniphyllate and (\pm)-Daphnilactone A.

McClure, K. F.; Benbow, J. W.; Danishefsky, S. J.; Schulte, G. K. *J. Am. Chem. Soc.* 1991, 113, 8185. A Novel Photochemical Route to the Mitomycins and FR-900482 Series.

McClure, K. F.; Danishefsky, S. J. *J. Org. Chem.* 1991 56, 850. Cycloaddition Reactions of Aromatic Nitro Compounds with Oxygenated Dienes. An Approach to the Synthesis of the FR-900482 Family of Antibiotics.

Ruggeri, R. B.; McClure, K. F.; Heathcock, C. H. *J. Am. Chem. Soc.* 1989, 111, 1530. Total Synthesis of (\pm)-Daphnilactone A: A Novel Fragmentation Reaction.

Unreviewed publication: Danishefsky, S. J.; Randolph, J.T.; Roberge, J. Y.; McClure, K. F.; Ruggeri, R. B. *Polymer Preprints* 1994, 35, 977. Application of the Glycal Assembly Method in the Solid-Phase: A New Strategy of Oligosaccharides and Glycoconjugates.

• PATENTS AND AND PATENT APPLICATIONS

Braganza, John Frederick; Letavic, Michael Anthony; McClure, Kim Francis. Preparation of triazolo[4,3-a]pyridines as MAP kinases, in particular p38 kinase inhibitors, and their use as antiinflammatory agents. WO 2004072072 A1

Dombroski, Mark Anthony; Letavic, Michael Anthony; McClure, Kim Francis. Preparation of 6-[4-(di- or trifluorophenyl)oxazol-5-yl][1,2,4]triazolo[4,3-a]pyridine as inhibitors of mitogen-activated protein (MAP) kinases. WO 2004020440 A1

Dombroski, Mark Anthony; Laird, Ellen Ruth; Letavic, Michael Anthony; McClure, Kim Francis. Preparation of novel benzotriazoles as anti-inflammatory compounds. EP 1247810 A1

Dombroski, Mark Anthony; Duplantier, Allen Jacob; Laird, Ellen Ruth; Letavic, Michael Anthony; McClure, Kim Francis. Preparation of 6-(phenylheterocyclyl)-[1,2,4]triazolo[4,3-a]pyridines as anti-inflammatory agents. WO 2002072579 A1

Dombroski, Mark Anthony; Letavic, Michael Anthony; McClure, Kim Francis. Preparation of 5-(phenylheteroaryl)-1,3-dihydro-2-benzimidazolone MAP-kinase inhibitors as anti-inflammatory agents. WO 2002072576 A1

McClure, Kim Francis; Robinson, Ralph Pelton, Jr. Preparation of 5-arylsulfonylaminocyclopentadioxole-5-hydroxamates as inhibitors of zinc metalloendopeptidases. EP 1041072 A1

McClure, Kim Francis; Noe, Mark Carl; Letavic, Michael Anthony; Chupak, Louis Stanley. Preparation of 4-phenylsulfonyl-3-morpholinehydroxamic acids and analogs as tumor necrosis factor α -convertase inhibitors. WO 0009492 A1

McClure, Kim Francis; Noe, Mark Carl; Letavic, Michael Anthony; Chupak, Louis Stanley. Preparation of hydroxy piperolate hydroxamic acid derivatives as MMP inhibitors. WO 0009485 A1

McClure, Kim Francis; Lopresti-Morrow, Lori Lynn; Mitchell, Peter Geoffrey; Reeves, Lisa Marie; Reiter, Lawrence Alan; Robinson, Ralph Pelton; Yocum, Sue Ann. Matrix metalloprotease (MMP)-13 selective

BEST AVAILABLE COPY

Vita for Kim F. McClure

inhibitors for treatment of arthritis deformans and other MMP-related diseases. JP 11199512 A2

McClure, Kim Francis. Preparation of N-arylsulfonylpiperidine-2-hydroxamic acids as matrix metalloproteinase and tumor necrosis factor production inhibitors. WO 9834918 A1

Robinson, Ralph Pelton, Jr.; McClure, Kim Francis. Preparation of arylsulfonylaminoalkylhydroxamates as inhibitors of matrix metalloproteinases or tumor necrosis factor production. WO 9833768 A1

• REFERENCES

Professor Daniel S. Kemp
Rm 18-582, Department of Chemistry
Massachusetts Institute of Technology
Cambridge, MA 02139
Phone (617) 253-1819
Fax (617) 253-0397
E-mail kemp@ucockatoo.mit.edu

Professor Clayton H. Heathcock
Department of Chemistry
University of California
Berkeley, CA 94720
Phone (510) 642-3360
Fax (510) 643-9480
E-mail chh@alkaloid.cchem.berkeley.edu

Professor Samuel J. Danishefsky
Department of Chemistry Columbia University
& Head of Laboratory of Bio-Organic Chemistry
Memorial Sloan-Kettering Institute for Cancer Research
1275 York Avenue, New York, NY 10021
Phone (212) 639-5501
Fax (212) 772-8691